

REMARKS

Claims 27-30, 33-40, 42-54, 59-68, 73-75, 84-85 and 90-104 are pending in the application.

Consideration of the following remarks is respectfully requested.

THE REJECTIONS UNDER 35 U.S.C. § 103(a) SHOULD BE WITHDRAWN

Claims 27-30, 33-36, 44-47, 59-68, 73-75, 90, 91 and 93 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lockhart et al., U.S. Patent No. 6,344,316 (“Lockhart”) in view of Bao et al., U.S. Patent No. 6,251,601 (“Bao”). Claims 37-40, 42, 43, 48-54, 84, 85, 90, 92 and 94-104 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lockhart in view of Bao as applied to claims 27, 67, 91 and 93 and further in view of Brown et al., U.S. Patent No. 5,807,522 (“Brown”). Applicant respectfully disagrees with the Examiner for the reasons presented below.

A finding of obviousness under 35 U.S.C. § 103(a) requires a determination that the differences between the claimed subject matter and the prior art are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere*, 383, U.S. 1 (1966). The relevant inquiry is whether the prior art suggests the invention and whether the prior art provides one of ordinary skill in the art with a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be found in the prior art. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). When a rejection depends on a combination of prior art references, there must be some teaching, suggestion, or motivation to combine the references. *In re Rouffet*, 149 F.3d 1350 (Fed. Cir. 1998).

At the outset, Applicant respectfully submits that none of the sections of Lockhart relied on by the Examiner in the instant Office Action supports the contention that Lockhart teaches comparing amounts of hybridization signal from a first sample, e.g., a specific hybridization sample, and a second sample, e.g., a non-specific hybridization sample, which, when combined with Bao, renders the present invention obvious. The Examiner points to Column 36, lines 24-47, of Lockhart for alleged support for such a contention. Applicant respectfully points out that the cited portion of Lockhart merely teaches selection of probes by evaluating the hybridization abilities of the probes to the target sample and, independently and separately, evaluating the hybridization abilities of the probes to the non-target sample. For example, selecting probes that show a strong hybridization signal with their target

involves comparing hybridization signals among different probes with their targets, whereas selecting probes that show little or no cross-hybridization involves comparing cross-hybridization signals among different probes with a second sample. As an example, Lockhart teaches selecting probes which show a strong signal as compared to their mismatch control: “[t]hus, only probes that show a strong signal compared to their mismatch control are selected” (Lockhart, Column 37, lines 11-12). As another example, Lockhart teaches using the hybridization data to develop a set of hybridization rules and using the cross-hybridization data to develop a set of cross-hybridization rules (Lockhart, Column 37, line 44, through Column 38, line 30). Thus, Lockhart does not teach or suggest combining the hybridization signal and cross-hybridization signal of the same probe into a single quantity, e.g., a ratio, and using such a single quantity as a measure of the binding property of the probe.

Applicant also respectfully points out that other sections of Lockhart that the Examiner cited in the instant Office Action do not teach or suggest presently claimed invention either. Specifically, Column 37, lines 5-12, of Lockhart teaches comparing the intensity difference between a probe and its mismatch control to the background signal intensity; and Column 70, line 58, through Column 73, line 46, of Lockhart teaches selection of probes in a two-step process, which is also based on intensity difference between a probe and its mismatch control: “[f]irst, in order to be counted, the difference in intensity between a probe and its corresponding mismatch probe had to exceed a threshold limit” and “[t]hen, the signal for a particular gene was counted as the average difference (perfect match--mismatch control) for the selected probes for each gene” (Lockhart, Column 71, lines 1-6 and lines 15-17, respectively). Applicant respectfully points out that a probe selection method utilizing the intensity difference between a probe and its mismatch control does not teach or suggest the presently claimed method.

Applicant further respectfully points out that, contrary to the Examiner’s contention, comparison to background level in Lockhart is not comparison to the hybridization level of a probe with the second sample. As a matter of fact, Lockhart teaches comparison to background level in its optional second round of selection (Lockhart, Column 37, lines 13-17 and lines 24-33), which involves hybridization with the “second sample,” i.e., a nucleic acid sample that is not expected to contain sequences complementary to the probes (Lockhart, Column 37, lines 14-17).

Having discussed the portions cited by the Examiner, Applicant reiterates that, as having been discussed in the response filed on December 26, 2002, nowhere does Lockhart teach or suggest combining the hybridization signal and cross-hybridization signal of a probe into a single quantity, e.g., a ratio, and using such a single quantity as a measure of the binding property of the probe as required by the instant independent claims.

Bao teaches a multi-color, comparative hybridization assay using an array of nucleic acid target elements attached to a solid support for the simultaneous detection of both gene expression and chromosomal abnormalities in a tissue sample. The method of Bao employs a comparative hybridization of a tissue mRNA or cDNA sample labeled in a first fluorescent color, a tissue chromosomal DNA sample labeled in a second fluorescent color, and at least one reference nucleic acid labeled in a third fluorescent color, to the array. The fluorescent color presence and intensity at each of at least two target elements are detected and the fluorescent ratios (i) of the first and third colors and (ii) the second and third colors determined. Bao does not teach or suggest evaluating a binding property of a polynucleotide probe. Nor does Bao teach or suggest using a ratio of the amount of hybridization by a first sample, e.g., a specific hybridization sample, to a polynucleotide probe and the amount of hybridization of by a second sample, e.g., a non-specific hybridization sample, to the polynucleotide probe as a measure of a binding property of the probe. As discussed above, nowhere does Lockhart teach or suggest combining the hybridization signal and cross-hybridization signal of a probe into a single quantity, e.g., a ratio, and using such a single quantity as a measure of the binding property of the probe as required by the instant independent claims. Thus, there is no teaching, suggestion, or motivation in Lockhart that its method can be combined with Bao as the Examiner contends. Furthermore, Applicant respectfully points out that Lockhart cannot be modified by Bao as suggested by the Examiner to give rise to the presently claimed invention in that, in Lockhart, hybridization data of a probe to the target sample and to the non-target sample are used independently and separately, e.g., for comparing hybridization signals between a probe and its mismatch control and for developing separate hybridization rules and cross-hybridization rules. Such methods cannot be practiced using a ratio between hybridization signal to the target sample and cross-hybridization signal to the non-target sample. As such, the rejection of claims 27, 67, 91 and 93, and claims dependent thereon, over Lockhart in view of Bao is erroneous, and should be withdrawn.

Brown teaches methods and apparatuses for forming microarrays of cDNAs on a support. Brown also teaches hybridization of nucleic acid samples to its microarrays. For example, in its example 1, Brown teaches hybridization to its microarray of two pools of nucleic acids, in which one pool contains random amplification products of the 6 large yeast chromosomes and the other pool contains random amplification products of the 10 small yeast chromosomes. The hybridization values of spots or clones on the array identify to which of the two pools the clones belong and correlate the clone to the location on the yeast genome (see, e.g., Brown, col. 17, lines 3-40). Brown does not teach or suggest evaluating a binding property of a polynucleotide probe. Nor does Brown teach or suggest using a ratio of the amount of hybridization by a first sample, e.g., a specific hybridization sample, to a polynucleotide probe and the amount of hybridization of by a second sample, e.g., a non-specific hybridization sample, to the polynucleotide probe as a measure of a binding property of the probe. The Examiner contends that Brown teaches a second sample comprising a deletion mutant, thereby supplementing a deficiency in Lockhart and Bao. Applicant respectfully submits that, as discussed above, the deficiency of Lockhart and Bao rests on the fact that they, alone or in combination, do not teach or suggest evaluating a binding property of a polynucleotide probe using a ratio of the amount of hybridization by a first sample, e.g., a specific hybridization sample, to a polynucleotide probe and the amount of hybridization of by a second sample, e.g., a non-specific hybridization sample, to the polynucleotide probe as a measure of a binding property of the probe. Thus, irrespective of whether Brown teaches a sample comprising a deletion mutant or not, Brown does not supplement what is missing in Lockhart and Bao. Applicant respectfully submits that the rejection of claims 37-40, 42, 43, 48-54, 84, 85, 90, 92 and 94-104 under 35 U.S.C. § 103(a) over Lockhart in view of Bao and further in view of Brown is erroneous, and should be withdrawn.

With respect to rejections of other dependent claims, Applicant respectfully points out that since Lockhart in view of Bao does not render independent claims 27, 67, 91 and 93 obvious, and Lockhart in view of Bao further in view of Brown does not render claims 37-40, 42, 43, 48-54, 84, 85, 90, 92 and 94-104 obvious, the rejection of the other dependent claims that depend on these claims cannot stand and should be withdrawn.

Therefore, Applicant respectfully submits that the rejection of claims 27-30, 33-36, 44-47, 59-68, 73-75, 90, 91 and 93 under 35 U.S.C. § 103(a) based on Lockhart in view of Bao and the rejection of claims 37-40, 42, 43, 48-54, 84, 85, 90, 92 and 94-104 under 35

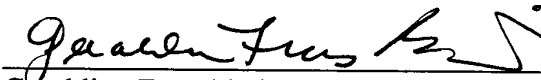
U.S.C. § 103(a) based on Lockhart in view of Bao and further in view of Brown should be withdrawn.

CONCLUSION

Applicant respectfully requests entry of the foregoing remarks into the file of the above-identified application. Applicant believes that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and allowance of the application are respectfully requested.

Respectfully submitted,

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Geraldine F. Baldwin 31,232
PENNIE & EDMONDS LLP (Reg. No.)
1155 Avenue of the Americas
New York, New York 10036-2711
(212) 790-9090